Section: Pathology

Original Research Article

INFLUENCE OF PATERNAL SMOKING ON PLATELET PARAMETERS IN WOMEN WITH SPONTANEOUS ABORTION

V. Keerthika[1], V. Sindu[2], Sreesupria. PR[3], A. Dhanalakshmi[4]

[1]Student, Coimbatore Medical College.
[2]Associate Professor, Department of Pathology, Coimbatore Medical College and Hospital, Coimbatore.
[3]Associate Professor, Department of Community Medicine, Government Medical College and ESIC, Coimbatore
[4]Professor, Department of Pathology, Coimbatore Medical College and Hospital, Coimbatore

Received : 10/11/2023
Received in revised form : 21/12/2023
Accepted : 09/01/2024

Keywords:
Miscarriage, MPV, Passive smoking, PDW, Platelet indices, P-LCR.

Corresponding Author:
Dr. A. Dhanalakshmi ,
Email: dhansupath@gmail.com

DOI: 10.47009/jamp.2024.6.1.150

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 768-774

Abstract

Background: Spontaneous abortion is the main widespread pregnancy complication and affects 15% of all pregnancies. A surprisingly high rate of passive smokers during pregnancy was found in a population in India (52%). Periconceptional paternal smoking termination is associated with 18% lower risk of spontaneous abortion. The most common mechanisms are chromosomal abnormalities in sperm and effects of chemicals like nicotine and carbon monoxide. The aim of this study is to find out whether platelet activation is seen pregnant women due to passive smoking and this, as a result of thrombosis, can be a cause of spontaneous abortion. The platelet activation is assessed by using platelet parameters like Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet Large Cell Ratio (P-LCR). **Materials and Methods:** Complete Blood Count was done using samples collected from pregnant women divided into 4 groups (cases of miscarriage and controls having a normal pregnancy, with a positive or negative passive smoking history). Platelet parameters were tabulated and analyzed using the unpaired t test. **Result:** On analysis, it is seen that MPV, PDW and P-LCR are increased in those who have been exposed to tobacco smoke and the increase is similar in cases and in controls. Also, a decrease in MPV is seen in aborted women, when compared to normal pregnancy, irrespective of passive smoking history. **Conclusion:** Platelet parameters are increased in passive smokers irrespective of pregnancy outcome. This shows that the effects on platelets is not a mechanism for spontaneous abortion in passive smokers.

INTRODUCTION

Spontaneous abortion is defined as clinically recognized pregnancy loss before 20thweek of gestation, as based on the last menstrual period.[1] "Passive smoking" is the phrase used to portray tobacco combustion products inhaled by non-smokers in the closeness of burning tobacco.[2]

It has been found that lethal metabolites of tobacco smoke are concentrated in the fetal blood in passive smokers.[3] It has been proved that passive smoking is a significant risk factor for abortion.[4] If this present pattern of smoking continues, WHO has reported that tobacco has the potential to cause around 10 million deaths per year from 2020 to 2030.[5]

Tobacco smoking causes platelet activation and changes its shape from discoid to spherical, thus increasing platelet parameters like MPV, PDW, P-LCR and Plateletcrit (PCT).[6] It has also been shown that MPV values were significantly increased in women with unexplained recurrent miscarriage, indicating thromboembolic etiology in miscarriage.[7] As passive smoking is equally disastrous to tobacco smoking, one should suspect that tobacco smoke inhalation can lead to platelet activation, thus increasing platelet parameters that could lead to miscarriage.

Therefore, in this study an attempt has been made to identify the association between paternal smoking, platelet activation and miscarriages by measuring platelet indices in pregnant women. If there is a link between paternal smoking and increased platelet indices in cases of miscarriage, we can try to prevent fetal loss in future through a simple cost-effective test, in women with smoking partners.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

MATERIALS AND METHODS

This is a case - control study. The cases are people suffering from miscarriage. The controls are people whose pregnancy is sustained beyond 20 weeks. The platelet parameters are compared between the cases and controls. The subjects are chosen from women attending antenatal outpatient clinic in the Department of Obstetrics and Gynecology in a tertiary care hospital. Ethical clearance was obtained in May and the study was done during June, July 2019.

In this study, 78 cases and 78 controls have been used. In cases, 33 subjects have a positive history of exposure to tobacco smoke while 45 subjects do not have history of exposure to tobacco smoke. In controls also, 33 subjects have a positive history of exposure to tobacco smoke while 45 subjects do not have history of exposure to tobacco smoke.

For cases, women aged 20-40 years with short period of amenorrhea, positive urinary HCG and uterine pregnancy previously confirmed by ultrasound, coming with a complain of bleeding from vagina and on ultrasound, absence of fetal heartbeat is noted. They should be lesser than twenty weeks of pregnancy. Such subjects are taken as cases.

The control group includes women whose pregnancy continues beyond 20 weeks of gestational age and the pregnancy should be ultrasonically confirmed. All women with diabetes mellitus, hypertension, thyroid disorders, abnormal anatomy of the uterus, ectopic pregnancies, on medication for any chronic illness or any other condition that might affect platelet count, are excluded. We have included women from 20 to 40 years because that age group is when women are reproductively most active.

Cases were identified in the antenatal outpatient clinic. Blood samples were collected in an EDTA vacutainer. Complete Blood Count (CBC) and the platelet parameters were analyzed immediately using automated hematology analyzer.

For controls, in those with gestational age less than 20 weeks, blood samples were collected in an EDTA vacutainer. Complete Blood Count and the platelet parameters were analyzed immediately using automated hematology analyzer. When their pregnancy continues beyond 20 weeks, these subjects become controls, irrespective of their pregnancy outcome. For those with gestational age more than 20 weeks, the data about the Complete Blood Count and platelet parameters done during the first trimester were collected from the subjects. History about their partner's smoking habits was collected through a questionnaire.

The data collected was tabulated in Microsoft Excel and analyzed using SPSS (Statistical Package for the Social Sciences) software. The statistical test used is the unpaired't' test. The platelet parameters in all the groups are expressed as mean ± standard deviation. t-test is used to test the significance between different groups. p value < 0.05 is considered to be statistically significant.

RESULTS

This case - control study was conducted in the Department of Pathology and the Department of Obstetrics and Gynecology with 78 cases and 78 controls (Table 1) in an attempt to check the difference in platelet parameters between aborted cases and normally pregnant subjects.

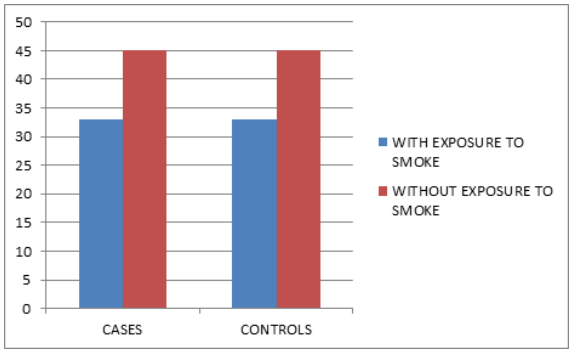

Figure 1: Sample size

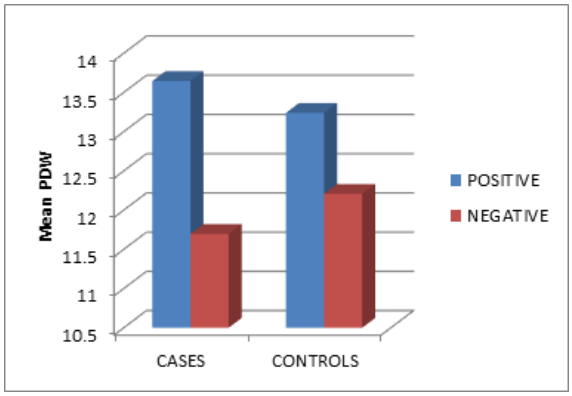

Figure 2: Comparison of PDW between 4 groups

In cases, the p value is 0.000. In controls the p value is 0.022

Both the p values are less than 0.05, hence it is statistically significant.

Therefore, exposure to tobacco smoke causes a significant increase in PDW in both cases and controls (Table 2) Since the p value for cases is less than 0.001, the association between exposure to tobacco smoke and PDW is stronger in cases than controls.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

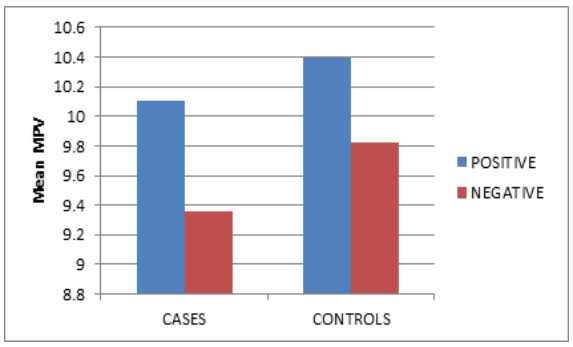

Figure 3: Comparison of MPV between 4 groups

p value for cases is 0.001 and for controls is 0.010. Both the values are less than 0.05 and hence are statistically significant.
Therefore, exposure to tobacco smoke causes a significant increase in MPV in both cases and controls (Table 3)

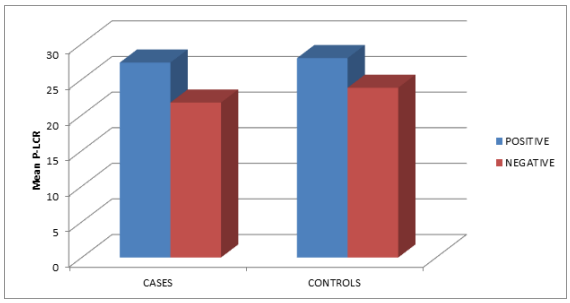

Figure 4: Comparison of P-LCR between 4 groups

p value for cases is 0.001 and for controls is 0.007. Both the values are less than 0.05 and hence are statistically significant. The significance is higher in cases.
Therefore, exposure to tobacco smoke significantly increases the P-LCR in both cases and controls (Table 4).

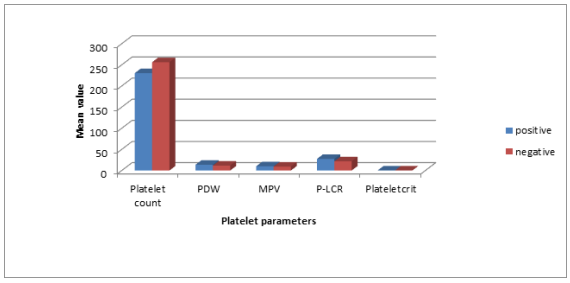

Figure 5: Comparison of platelet parameters between cases with a positive and negative history of passive smoking

From table 5, the p value of platelet count is 0.079 and plateletcrit is 0.755. It is greater than 0.05, hence there is no effect of passive smoking on platelet count and plateletcrit in cases.

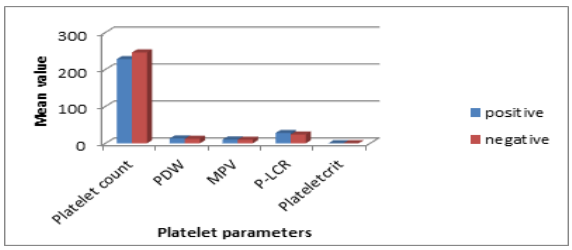

Figure 6: Comparison of platelet parameters between controls with a positive and negative history of passive smoking

From table 6, the p value of platelet count is 0.262 and plateletcrit is 0.903. It is >0.05, hence there is no effect of passive smoking on platelet count and plateletcrit in controls.

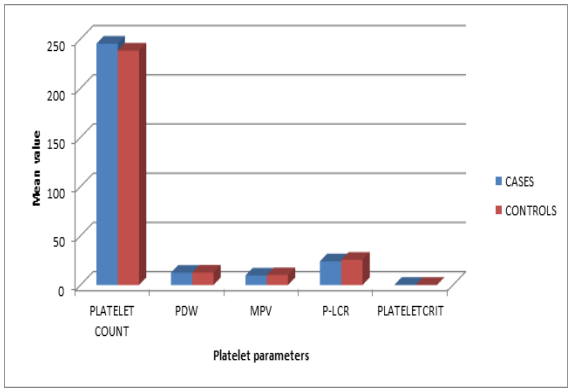

Figure 7: Comparison of platelet parameters between cases and controls

From table 7, we can see that only MPV has significantly changed between cases and controls. The p value is 0.013. MPV is significantly decreased in cases of spontaneous abortion.

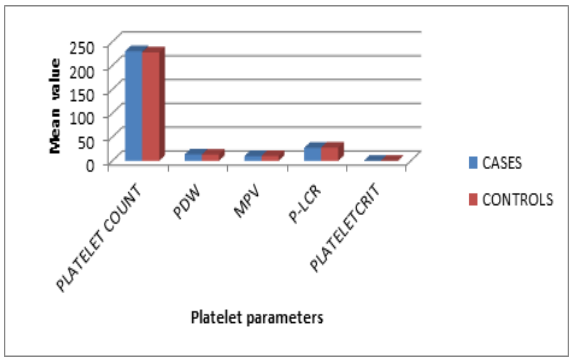

Figure 8: Comparison of platelet parameters between cases and controls exposed to tobacco smoke.

From table 8, it is clear that none of the values are statistically significant. p value for all parameters is >0.05 Hence exposure to tobacco smoke causes an increase in platelet parameters (MPV, PDW and P-LCR) which is similar in cases and controls.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Number of samples

	Cases	Controls
With exposure to smoke	33	33
Without exposure to smoke	45	45
Total	78	78

Table 2: Platelet distribution width

Exposure to tobacco smoke	Cases		Controls	
	Mean	Std. Deviation	Mean	Std. Deviation
Positive	13.6455	2.14841	13.2394	1.94373
Negative	11.6956	1.71026	12.2067	1.90256

Table 3: Mean platelet volume

Exposure to tobacco smoke	Cases		Controls	
	MEAN	STD. DEVIATION	MEAN	STD. DEVIATION
Positive	10.1030	1.00234	10.3970	.93324
Negative	9.3578	.84356	9.8244	.94584

Table 4: Platelet large cell ratio

Exposure to tobacco smoke	Cases		Controls	
	MEAN	STD. DEVIATION	MEAN	STD. DEVIATION
Positive	27.3606	7.17674	27.9848	6.12429
Negative	21.7489	6.47101	23.8267	6.76651

Table 5: Platelet parameters in cases

	With exposure to smoke	Without exposure to smoke	P value
	Mean±std. Deviation	Mean±std. Deviation	
Platelet count	230.3030±62.24372	256.2444±64.58896	0.079
PDW	13.6455±2.14841	11.6956±1.71026	0.000
MPV	10.1030±1.00234	9.3578±.84356	0.001
P-LCR	27.3606±7.17674	21.7489±6.47101	0.001
Plateletcrit	0.2276±.06144	0.2318±.05614	0.755

Table 6: Platelet parameters in controls

	With exposure to smoke	Without exposure to smoke	P value
	Mean±std. Deviation	Mean±std. Deviation	
Platelet Count	227.9091±67.37134	245.7778±70.03664	0.262
PDW	13.2394±1.94373	12.2067±1.90256	0.022
MPV	10.3970±.93324	9.8244±.94584	0.010
P-LCR	27.9848±6.12429	23.8267±6.76651	0.007
Plateletcrit	0.2333±.06343	0.2351±.06359	0.903

Table 7: Comparison of platelet parameters between cases and controls

	Cases	Controls	p value
	MEAN±STD. DEVIATION	MEAN±STD. DEVIATION	
Platelet Count	245.2692±64.50061	238.2179±69.05196	0.511
PDW	12.5205±2.12831	12.6436±1.97541	0.709
MPV	9.6731±0.98055	10.0667±0.97683	0.013
P-LCR	24.1231±7.28829	25.5859±6.78422	0.196
Plateletcrit	0.2300±0.05809	0.2344±0.06311	0.654

Table 8: Comparison of platelet parameters of cases and controls exposed to tobacco smoke

	Cases	Controls	p value
	Mean±STD. Deviation	Mean±STD. Deviation	
Platelet count	230.3030±62.24372	227.9091±67.37134	0.881
PDW	13.6455±2.14841	13.2394±1.94373	0.424
MPV	10.1030±1.00234	10.3970±.93324	0.222
P-LCR	27.3606±7.17674	27.9848±6.12429	0.705
Plateletcrit	0.2276±.06144	0.2333±.06343	0.709

DISCUSSION

Second hand tobacco smoke exposure from the partner at or around the time of conception or during gestation is proved to have significant effects on the pregnancy outcome in the form of spontaneous abortion, stillbirths and tubal ectopic pregnancy.[8] The increased risk of health hazards associated with exposure to passive smoke is about one third as that of active smoking.[9,10]

The already known mechanisms for the relationship between paternal smoking and miscarriages are:

1. Chromosomal abnormalities in sperm,[11]
2. Nicotine

ISSN (O): 2687-5365; ISSN (P): 2753-6556

- Acts on the heart and blood vessels causing the release of catecholamines into the blood of the mother, and therefore causing tachycardia, peripheral vasoconstriction and decrease of placental blood flow, resulting in reduced nutritional and oxygenation rates for the fetus.[12]
- It also causes an imbalance between vasodilating antiplatelet prostacyclin and the vasoconstricting platelet aggregating thromboxane A2, which is released from the platelets 9.
- Cotinine , a metabolite of nicotine, enhances the vasocontrictive action of prostaglandin E2 12.

3. Carbon monoxide has a strong affinity towards fetal hemoglobin. This shifts the oxygen-hemoglobin saturation curve towards the left, and reduces the blood oxygen transportation capacity, thus leading to fetal hypoxia and thereby spontaneous abortion.[12]

In our study, 78 cases and 78 controls have been compared with 33 subjects in each group having a positive history of exposure to cigarette smoke [Table 1 and Figure 1]. We have analyzed whether the platelet activation due to passive smoking can lead to spontaneous abortion in women with active smoking partners.

To measure platelet activation, advanced markers like β-thromboglobulin or soluble platelet P-selectin can be assessed. But this process is more time-consuming, expensive and they cannot be performed as a part of the regular laboratory tests.[6,13,14] As an alternative, platelet indices, which are markers of platelet activation, have been measured through a cost-effective, easy and a regularly used lab test (complete blood count).[6]

In our study, in [Table 2], a significant increase in PDW is seen in passive smokers in both cases and controls. In cases the p value is 0.000 and in controls the p value is 0.022. [Figure 2] shows that there is a strong correlation between PDW and passive smoking in cases than in controls. This is similar to the study done by Tulgar et al,[15] who found out that there was a significant increase in PDW in smokers when compared to non smokers with a p value of 0.010.

In this study, according to [Table 3], a significant increase in MPV is noted in passive smokers. In cases, (p value: 0.001) the association is stronger than in controls (p value: 0.010), as is evident from Figure 3. This is in accordance with the study done by Ercan Varol et al,[16] who compared platelet indices between 116 smokers and 90 non-smokers and found a significant rise in MPV in smokers (p value <0.001). Tulgar et al,[15] found similar results (9.11±0.86 in smokers vs. 9.03±0.92 in non-smokers) with a p value of 0.637. Similarly, Ghahremanfard et al,[17] found an increase in MPV in smokers (9.9±1.1 vs. 9.8±1.2) with a p value of 0.615.On the contrary, Butkiewicz et al,[18] and Erol Arslan et al,[19] showed no difference in MPV between smokers and non-smokers.

The present study reveals that there is a significant increase in P-LCR [Table4] in passive smokers when compared to non smokers (cases- p value: 0.001; controls - p value: 0.007), as seen in [Figure 4]. Swaminathan A et al,[6]found that there was no significant difference in P-LCR between smokers and non- smokers (p value: 0.697), but they found out that P-LCR significantly increases as the duration and intensity of smoking increases (p value: 0.004).Osama Awad Ahmed 5 compared 35 smokers and 30 non- smokers and found that there was no significant change in P-LCR. (p value:0.626).

Hence, markers of platelet activation like MPV, PDW and P-LCR are significantly increased in women exposed to tobacco smoke from partners. This may be due to:

1. Thrombosis:

Thrombosis increases the demand for platelets leading to release of immature platelets from bone marrow. These are larger in size.

2. Due to increased activity of PAF[9]:

The chemicals in cigarette smoke inhibit the action of the enzyme acetyl hydrolaze that is present in human plasma. The action of this enzyme is to inactivate the platelet activating factor (PAF) by converting PAF to lyso-PAF by specifically removing the acetyl group at the sn-2 position of PAF20. To obtain a larger surface, platelets change in shape from discoid to spherical during activation. Pseudopodia are formed hence platelets appear larger.[21]

PDW can be increased as a result of more young platelets being released into circulation leading to variation in size of platelets.[5,6]

In the present study, from [Figures 5 and 6], it is clear that there is no significant change in platelet count (p value: cases- 0.079, controls-0.262) and plateletcrit (p value: cases-0.755; controls-0.903) due to passive smoking, in both cases and controls [Tables 5 and 6]. This is in accordance to the study done by Tulgar et al,[15] that showed no significant effect on platelet count and plateletcrit in smokers. In contrast to this, the study done by Ghahremanfard F,[17] showed a significant increase in platelet count in smokers (p value: 0.021). However, in our study, the mean platelet count is decreased. This is probably due to increased consumption of platelets due to thrombosis.

When the platelet parameters of cases and controls were compared irrespective of smoking history, no significant difference was found in platelet parameters, except MPV (p value:0.013), which is reduced in cases [Table 7 and Figure 7]. This is similar to the study done by Funda Yildrim Bas1 who proved that MPV can be used as a negative predictive marker of spontaneous abortion (p value: <0.001). The mechanism of decrease in MPV in spontaneous abortion is not known.

When the platelet parameters of cases and controls exposed to tobacco smoke were compared, the increase in platelet parameters was not significantly

ISSN (O): 2687-5365; ISSN (P): 2753-6556

different in both the groups. (p value >0.05 for all platelet indices, [Table 8 and Figure 8]). So, in our study, we did not find a link between platelet activation due to passive smoking, and abortion. But the passive smoking history, obtained by self reports of the women might not be very accurate, the sample size is very small, and the controls were followed up only for a period of two months because of very short study duration, hence the pregnancy outcome is unknown. With these limitations, we cannot confirm that the effect of passive smoking on platelets is not the underlying mechanism of spontaneous abortion.

CONCLUSION

From this study, we have concluded that exposure to cigarette smoke causes platelet activation in pregnant women (increase in MPV, PDW and P-LCR), but this is not a possible mechanism of spontaneous abortion. But further research in this field, by measuring the maternal blood levels of chemicals in tobacco smoke like cotinine and carbon monoxide is necessary to more accurately assess the effect of passive smoking on platelets and its adverse pregnancy outcomes. If it is found that thrombosis due to platelet activation because of passive smoking in pregnant women can result in spontaneous abortion, high risk pregnancies can be identified and fetal loss can be prevented by doing this simple, affordable blood test (CBC).

We can also counsel the smoking partners to quit smoking for the welfare of the mother and the child.

We have also concluded that MPV is decreased in cases of abortion when compared to normal pregnancy, irrespective of smoking history, for which the mechanism is still unknown. So further research work is necessary to find out the pathogenesis of decreased MPV in spontaneous abortion.

Acknowledgements

I thank the Almighty for his blessings in completing this project. I express my sincere gratitude to The Indian Council of Medical Research (ICMR) for giving me an opportunity to carry out this study under the Short-Term Studentship Programme 2019 (STS-2019). I thank my guide for her valuable guidance and indispensable help. I am obliged to take this opportunity to thank all the teaching and the non-teaching staff of my institution, and the patients for their co-operation throughout the period of study. Last but not the least; I extend my sincere thanks to my family and friends who helped me through this project.

REFERENCES

1. Bas FY, Tola EN, Sak S, Cankaya BA. The role of complete blood inflammation markers in the prediction of spontaneous abortion. Pak J Med Sci 2018;34:1381-5.
2. Teruo Inoue. Cigarette smoking as a risk factor of coronary artery disease and its effects on platelet function. Tob Induc Dis 2004;2:27-33.
3. Meeker JD, Missmer SA, Cramer DW, Hauser R. Maternal exposure to second hand tobacco smoke and pregnancy outcome among couples undergoing assisted reproduction. Hum Reprod 2007;22:337-45.
4. Wang L, Yang Y, Liu F, Yang A, Xu Q, Wang Q, et al. Paternal smoking and spontaneous abortion: a population-based retrospective cohort study among non-smoking women aged 20-49 years in rural china. J Epidemiol Community Health 2018;72:783-9.
5. Osamah Awad Ahmed. Effects of smoking cigarette on white blood cell and platelet parameters on a sample of normal subject in Rania city. Imperial journal of interdisciplinary research 2016;2:887-90.
6. Swaminathan A, Amitkumar K, Ganapathy S, Ayyavoo S. Evaluation of the impact of cigarette smoking on platelet parameters. Natl J Physiol Pharm Pharmacol 2015;5:426-30.
7. Yilmaz M, Delibad IB, Isaoglu U, Ingec M, Borekci B, Ulug P. Relationship between mean platelet volume and recurrent miscarriage: a preliminary study. Arch Med Sci 2015;11:989-93.
8. Hyland A, Piazza KM, Hovey KM, Ockene JK, Andrews CA, Rivard C, et al. Associations of lifetime active and passive smoking with spontaneous abortion, stillbirth and tubal ectopic pregnancy: a cross-sectional analysis of historical data from the Women's health initiative. Tob Control 2015;24:328-35.
9. Yarlioglues M, Ardic I, Dogdu O, Akpek M, Zencir C, Kasapkara HA, et al. The acute effects of passive smoking on mean platelet volume in healthy volunteers. Angiology 2012;63:353-7.
10. Raupach T, Schafer K, Konstantinides S, Andreas S. Second hand smoke as an acute threat for the cardiovascular system: a change in paradigm. Eur Heart J 2006;27:386-392.
11. Beal M A, Yauk C L, Marchetti F. From sperm to offspring: Assessing the heritable genetic consequences of paternal smoking and potential public health impacts. Mutat Res 2017;773:26-50.
12. Nakamura MU, Alexandre SM, Santos JFK, de Souza E, Sass N, Beck APA, et al. Obstetric and perinatal effects of active and/or passive smoking during pregnancy. Sao Paulo Med J 2004;122:94-8.
13. Dundar O, Pektas MK, Bodur S, Bakir LV, Cetin A. Recurrent pregnancy loss is associated with increased red cell distribution width and platelet distribution width. J Obstet Gynecol Res 2015;41:551-8.
14. Vagdalti E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Librianou I. Platelet Distribution Width: a simple, practical and specific marker of activation of coagulation. Hippokratia 2010;14:28-32.
15. Tulgar Y K, Cakar S, Tulgar S, Dalkilic O, Cakiroglu B, Uyanik BS. The effect of smoking on neutrophil/lymphocyte and platelet/lymphocyte ratio and platelet indices: a retrospective study. Eur Rev Med Pharmacol Sci 2016;20:3112-8.
16. Varol E, Icli A, Kocyigit S, Erdogan G, Ozydin M, Dogan A. Effect of smoking cessation on Mean Platelet Volume. Clin Appl Thromb Hemost 2013;19:315-9.
17. Ghahremanfard F, Semnani V, Ghorbani R, Malek F, Behzadfar A, Zahmatkesh M. Effects of cigarette smoking on morphological features of platelets in healthy men. Saudi Med J 2015;36:847-50.
18. Butkiewicz AM, Kemona-Cheynik I, Dymicka-Piekarsha V, Matowicka Karna J, Kemona H, Radziwon P. Does smoking affect thrombocytopoiesis and platelet activation in men and women? Adv Med Sci 2006;51:123-6.
19. Arslan E, Yakar T, Yavasoglu I. The effect of smoking on mean platelet volume and lipid profile in young male subjects. Anadolu Kardiyol Derg 2008;8:422-5.
20. Ambrosio G, Oriente G A, Napoli C, Palumbo G, Chiarello P, Marone G, et al. Oxygen Radicals Inhibit Human Plasma Acetylhydrolase, the Enzyme That Catabolizes Platelet-activating Factor. J Clin Invest 1994;93:2408–16.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

21. Etheresia Pretorius. Ultrastructural changes in platelet membranes due to cigarette smoking. Ultrastruct Pathol 2012;36:239-43.
22. Larsen E C, Christiansen O B, Kolte A M, Macklon N. New insights into mechanisms behind miscarriage. BMC Medicine 2013;11.
23. Amirkhani J, Yadollah-Damavandi S, Mirlohi SM, Nasiri SM, Parsa Y, Ghahrehbeglou M. Correlation between abortion and infertility among non-smoking women with a history of passive smoking in childhood and adolescence. International journal of reproductive medicine 2014.
24. Meeker JD, Missmer SA, Vitonis AF, Cramer DW, Houser R. Risk of spontaneous abortion in women with childhood exposure to parental cigarette smoke. Am J Epidemiol 2007;166:571-5.
25. Koupenova M, Kehrel EB, Corkrey HA, Freedman JE. Thrombosis and platelets: an update. Eur Heart J 2017;38:785-91.
26. Bick RL. Recurrent miscarriage syndrome and infertility caused by blood coagulation protein or platelet defects. Hematol Oncol Clin North Am 2000;14:1117-31.
27. Redline RW. Thrombophilia and placental pathology. Clin Obstet Gynecol 2006;49:885-94.
28. Hafes AS, Fahim HI, Badawy HA. Socioenvironmental predictors of abortion and stillbirths in an industrial community in Egypt. J Egypt Public Health Assoc 2001;76:1-16.
29. Venners SA, Wang X, Chen C, Wang L, Cheng D, Guang W, et al. Paternal smoking and pregnancy loss: A prospective study using a bio-marker of pregnancy. Am J Epidemiol 2004;159:993-1001.
30. Erikssen J, Hellem A, Stormorken H. Chronic effect of smoking on platelet count and "platelet adhesiveness" in presumably healthy middle-aged men. Thromb Haemost 1977;38:606-11.
31. Al-Aghbary AAR, Almorish MAW, Jaffar DWM, Al-Kahiry WM. Platelet indices in evaluation of patients with recurrent pregnancy loss. Asian Pacific Journal of Reproduction 2018;7:15-8.
32. Bezerra de Mello PR, Pinto GR, Botelho C. Influence of smoking on fertility, gestation and lactation. J Pediatr 2001;77:257-64.

ISSN (O): 2687-5365; ISSN (P): 2753-6556